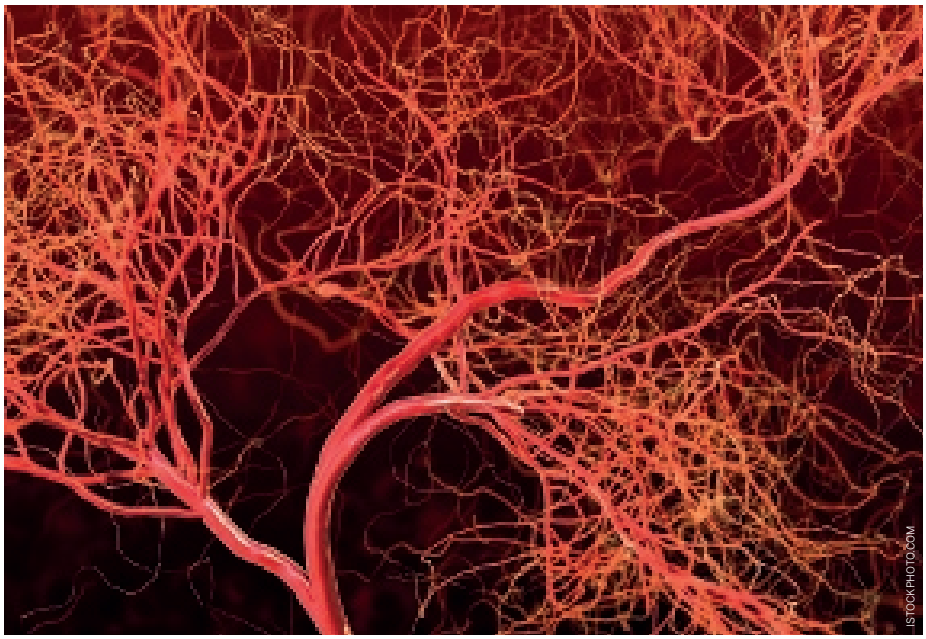

Dilation in molecular detail

This year's Ariëns Award winner is Susan Brain. At the Dutch Medicines Days, she will receive the award for her work on TRP channels and the vasodilator activity of CGRP. 'An orally available CGRP agonist could be a new drug against cardiovascular disease.'

The Dutch Society for Pharmacology (NVF) has recognised the work of outstanding international pharmacologists since 1985 with the annual Ariëns Award, named in honour of the Dutch professor Everhardus Jacobus Ariëns, one of the founders of the field of pharmacology. This year's Award winner is Susan Brain, Professor of Pharmacology at the Cardiovascular Division and Pharmacology Department at King's College in London. 'I must admit I was surprised and delighted when I heard that I'd be receiving this award. Fantastic!'

Brain has published over 180 research papers. She is probably best known for her discovery in the 1980s that calcitonin gene-related peptide (CGRP), a neuropeptide, is a potent vasodilator. 'I was studying skin when we realised this important feature of CGRP', says Brain. 'Others then discovered that CGRP is released in migraine. This led to the development of GCRP antagonists and antibodies that are known to benefit migraine and are now used in clinical trials.'
One of Brain's research goals is to decipher the effect of CGRP on blood pressure in humans. 'When something causes blood pressure to increase there will be stress on the blood vessels. This appears to signal sensory nerves to release CGRP at the level of the blood vessel, which then in turn lowers blood pressure. That is a least what we think happens based on our studies in rodents', she says.
CGRP can be released due to activation of the so-called transient receptor potential (TRP) channels on the endings of sensory nerves. 'There are several families of TRP channels, all responding to a range of different stimuli', explains Brain, 'for instance in thermoregulation.' She has worked out signalling pathways in mice to show that when the environment is painfully cold, activation of TRP-A1 channels leads to vasoconstriction in the skin, preventing heat loss. 'TRP-A1 is involved in this response and also in the subsequent dilator response. It is important to study these mechanisms in humans because many people, especially the elderly, die because of the cold. It is possible that TRP-A1 channel signalling is disturbed in older people.'

'This signalling may be disturbed in older people'

Inflammation

The TRP-A1 channel also seems to be involved in arthritis. 'The TRP-A1 channels on the sensory nerves near the inflamed site are activated and help cause the pain', explains Brain. 'When the patient is cold there is even more activation and consequently more pain. TRP-A1 channel blockers have been made and turn out to alleviate pain in rodents; we are waiting to see what happens in arthritis patients. We are also wondering if we can make a CGRP mimetic, which can serve as a new drug that can regulate blood pressure and help treat cardiovascular disease.'
And this is just the beginning, says Brain: 'There are actually about 28 TRP channels. We would like to study some of them. There is definitely a great deal more to discover!' ●